Off-pump left ventricle reconstruction using the Revivent Myocardial Anchoring System in patients with severe ischemic cardiomyopathy.

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To study patients with severe HF who would benefit from off-pump SVR using the Revivent Myocardial Anchoring System. To investigate the characteristics of the ischaemic heart using CMR or cardiac CT in order to verify patient eligibility for the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON44507

Source
ToetsingOnline

Brief title
Off-pump SVR in ischaemic heart failure.

Condition

- Heart failures
- Cardiac therapeutic procedures

Synonym
Ischaemic cardiomyopathy, ischaemic heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 1. Severe ischemic cardiomyopathy, 2. Left ventricle dilatation and low ejection fraction., 3. Off-pump left ventricular, reconstruction

Outcome measures

Primary outcome

The main study endpoints are:

- Assessment of complications over the course of 1 year

- Evaluation of the decrease in LV volume by measuring the LVESVI with

MRI/CT, (6) and 12 months after surgery

- Evaluation of changes in heart failure status measured by NYHA class, quality

of life assessment questionnaire and ergometry/6MWT. These data will be

collected at the beginning of the study and at the 6th and 12th month of the

follow-up

- Compilation of detailed description of ischaemic heart characteristics

using MRI (before the procedure , 6 and 12 months postoperatively) or cardiac

CT (before and 12 months after the procedure).

- MRI/CT quantification of DMF in the non-infarcted myocardium at the beginning

and end of the study

- Assessment of LVEF improvement with TTE/MRI or CT, prior to surgery and during follow-up

- Assessment of any improvement in mitral valve regurgitation within 1 year , measured at several time intervals (preoperatively, intraoperatively, at discharge, and 6 and 12 months postoperatively).

Secondary outcome

The secondary endpoints are:

- Gathering of clinical information that is potentially relevant for the study objectives, including comorbidities, fluid status and medication use

- Assessment of diastolic function with TTE (preoperatively, at discharge, 6 and 12 months after surgery).

- Evaluation of procedure-related ischaemia(ECG alternation and/or increase in CKMB level) intra-operative and for 48 hours postoperatively

- Record the biomarker profile (NT-proBNP, trop I, Gal-3 and creatinine)

- 48 hour postoperative Holter monitoring for arrhythmias

- Intra-operative documentation of heart characteristics by means of TEE (LV volume, function , mitral valve regurgitation, tethering area, coaptation depth)

- Record number of patients with LAA exclusion in combination with SVR.

Study description

Background summary

In western countries, heart failure is a major health issue. The combination of an aging population and more effective treatment of its precursor - MI - make heart failure (HF) a growing health problem. Improved reperfusion therapy, by means of catheterization (PCI), in the acute stage of myocardial infarction (MI) and standardized use of post-infarction cardioprotective medication has led to a sharp decline in mortality. As a result, the incidence of patients with ischaemic cardiomyopathy (ICM) has increased. In the western world, the prevalence of HF can be estimated at 1-2% and its incidence is 5-10 per 1000 persons per year. Left ventricular remodelling, a pathological process that follows MI, occurs in more than 30% of patients treated with acute reperfusion therapies and cardioprotective medications. Cardiac remodelling is a process which leads to alteration in the size, shape, structure and function of the ventricles. Remodelling in non-infarcted myocardium is initiated and sustained by chronic haemodynamic stresses on the heart. As a result, the failing heart becomes less elliptical and more spherical. The heart enlarges to increase ventricular volume which leads to greater systolic volume and higher cardiac output despite reduced ejection fraction (EF). Remodelling is also characterized by gradual accumulation of DMF in non-infarcted myocardium. Left ventricular remodelling is associated with progression of HF and a poor prognosis. Another adverse effect of LV enlargement is mitral valve regurgitation. Ischaemic mitral valve insufficiency is a ventricular problem and is associated with progression to heart failure.

The gold standard modality used to quantify the extent of postischaemic scarring, DMF and remodelling, is cardiovascular magnetic resonance imaging (CMR). Various parameters that are used to evaluate heart failure are measured using CMR. A powerful marker of LV remodelling is the left ventricular (LV) end-systolic volume indexed to body surface area (ESVI). An LVESVI >60ml/m2 (normal =25ml/m2) is associated with a fivefold increase in mortality. It is a valuable predictor of hospitalization for heart failure, even in patients

with a normal ejection fraction (EF) . The most commonly used index for left ventricular function, is the EF. Two important mechanisms underlying heart failure with reduced EF are: poor contractile function due to extensive myocardial damage and LV dilatation caused by infarct expansion and stretching of the myocardial scar. A left ventricular EF < 40% is associated with impaired LV function.The alternative for CMR is the cardiac CTA. The cardiac CTA has a good correlation with MRI in measurement of LV volume, LVEF and extent of postischaemic scar. Most of the patients who meet the inclusion criteria of this study, have a cardiac device. Ischaemic mitral valve insufficiency, which affects 25% of patients after MI, results from annular dilatation and remodelling of the subvalvular apparatus. The presence of even mild mitral insufficiency is associated with reduced survival rates.

The N-terminal prohormone of brain natriuretic peptide (NT-proBNP), troponin I (trop I), galectin-3 (Gal-3) and creatinine are important biomarkers of heart failure. The biomarker profile of a patient has prognostic importance and correlates with the severity of heart failure. Furthermore, diastolic dysfunction can be found in a heart failure population with normal or preserved left ventricular EF .
Patients with ischaemic heart failure are at high long-term risk for morbidity and mortality. Heart failure leads to shortness of breath, fatigue and reduced exercise capacity as a result of LV dysfunction. Pulmonary congestion, dysrhythmia and peripheral oedema occur as HF progresses. The elderly are primarily affected by this chronic disease and it is one of the main causes of hospitalization in this group of patients . Among this population, the 5-year mortality is 50-77%, with sudden cardiac death or uncontrolled symptoms of heart failure being the predominant cause of death. Recent HF guidelines accentuated the importance of the early identification of high risk patients for morbidity and mortality from HF, not only for prevention and effective treatment but also for regulation of healthcare costs associated with treatment of this group of patients.

The medical management of ischaemic HF includes: heart failure medications, cardiac-assist devices, heart transplantation and left ventricular assist devices (LVADs). These are important therapies for ischaemic HF, but are beyond the scope of this study and will not be discussed in detail.

1. Surgical Ventricular Reconstruction
Surgical ventricular reconstruction (SVR) can be used to treat ischaemic heart failure due to systolic dysfunction following anterior MI and LV dilatation. By excluding the MI scar, the relationship between function and structure is restored. SVR rebuilds the failing heart to reconstruct the natural elliptical configuration from the dilated spherical form. This procedure is often performed concomitantly with an intervention on vessels and valves. The early and late benefits of SVR have been consistently reported in various studies. Although refuted in randomized trials, this procedure results in definitive improvements in QoL .

There are various approaches to SVR but these will not be discussed as they are beyond the scope of this study.

2. Revivent Myocardial Anchoring System
The Revivent device was developed by BioVentrix and obtained the CE mark in 2012. This device has been developed to reconstruct the LV in a minimally invasive way in patients with ischaemic cardiomyopathy. The study performed in order to obtain the CE mark for this new technique has already shown favourable results. The Revivent System has been implanted in 60 patients with ischaemic HF. Results obtained after 1 year showed a reduction of 35% in LVESVI, a 15% improvement in LVEF, a one grade reduction in NYHA classification, a 20% improvement in 6-minute walking scores, and a 32% improvement in quality of life scores.

Study objective

To study patients with severe HF who would benefit from off-pump SVR using the Revivent Myocardial Anchoring System. To investigate the characteristics of the ischaemic heart using CMR or cardiac CT in order to verify patient eligibility for the Revivent System. To analyze the characteristics of patients with severe ICM who would profit from the less-invasive SVR with Revivent System.

Study design

The study will be a prospective, non-randomized , single-armed cohort study of patients with ischaemic HF. It is designed to investigate the new less-invasive technique for LV reconstruction. During a follow-up period of 1 year, patient outcomes after the Revivent System implantation will be monitored. Patients giving informed consent agree to the implantation of the Revivent System and will undergo clinical tests at certain intervals (prior to the operation, during the procedure and hospital admission, at discharge, 30 days, 6 and 12 months after the surgery). Patients will also consent to the collection of clinical data at these intervals. This study will have no control group.

Intervention

The Revivent device will be used for surgical restoration of left ventricle. This device can be used to place permanent cardiac implants into the heart for the reduction of the LV volume in patients with ischaemic heart failure. The system utilizes anchors that are implanted into the scarred area of the heart, which, when deployed, exclude some of the scarred area from the ischaemic event. This procedure is performed in a surgical setting without the use of cardiopulmonary bypass. The Revivent components consist of a series of catheters and anchors that are deployed under fluoroscopic imaging and TEE. The implantation of the Revivent device can be performed as a stand-alone procedure

through sternotomy or in combination with other cardiac surgery.

This technique needs no cardiac incision and allows major reconstruction of the LV on a beating heart in a short time span.

The Revivent System consists of implantable components and a series of anchors. The anchor pairs are connected to each other by an adjustable *length Tether. The distance between anchors is variable and determined by the position of the Locking Anchor on the Tether. The Hinged Anchor is hinged to facilitate low-profile passage through a catheter that is inserted perpendicularly to the septum, after which it can be pivoted 90° to lie flat on the septum; the Locking Anchor houses a cam-based reversible locking mechanism allowing apposition of the two anchors at a continuum of positions. Once the proper distance between the two is established, excess Tether length is cut and removed.

Study burden and risks

Cardiac CTA: balancing risks and benefits

Patients undergoing a cardiac CTA are exposed to a high radiation dose. Radiation dose exposure has been associated to an increased risk of developing a radiation-induced cancer 27,28. Therefore, the potential benefit of CTA for assessment of cardiac function and shape have to be carefully weighed against the potential risks.
Cardiac CTA is a non-invasive, patient-friendly imaging modality to investigate LV geometry and function but require a high dose of radiation. For this reason, in this study the cardiac CTA will be performed only by patients with MRI incompatible ICD*s or CRT*s. Unlike the MRI group, the operation indication will be determined by means of the already existing imaging. Due to potential risk of cardiac CTA, all efforts will be made to ensure that the most eligible candidates for the operation undergo the CTA. Basically, patients undergoing a cardiac CTA will undergo the operation. Patients with a cardiac device and yet meeting the inclusion criteria are at the end stage of heart failure. Though, there is a potential risk attached to cardiac CTA, the surgical team believe that they will benefit from the operation. The potential benefit of minimal invasive SVR and potential risk of radiation will be assessed for each individual patient. All efforts will be made to recruit patients with a MRI-compatible cardiac device to avoid the use of ionizing radiation. In the worst case, the cardiac CTA has to be performed by the whole study population (n=10). The potential lifetime-attributable risk (LAR) of cancer for cardiac CTA differs considerably with age and sex 28. The LAR is high for younger age, women (due to risk of breast cancer in addition to lung cancer) and for combined cardiac and aortic scanning. The risk is markedly lower for old patients due to declined radiosensitivity of many organs and the long latency period from radiation exposure to development of malignancy. It is important to

take the potential risk of dying from cancer in perspective relative to the poor prognosis of advanced heart failure. Furthermore, most of the eligible candidates with advanced heart failure are above the age of 60,which is a less vulnerable group of patients for radiation-induced cancer. The standard exclusion criteria for cardiac CTA like renal dysfunction, intolerance for iodinated contrast, contraindication for *-blocker, rapid ventricular response during atrial fibrillation and frequent atrial or ventricular arrhythmias will be taken in account while selecting these patients.
To reduce radiation exposure, the CTA will be performed only at the beginning and end of the study. Prior to the operation, it is significant to image the function and dimension of the left ventricle. Accurate measurements of the LV and localisation of the postischaemic scar are extremely important for the LV reconstruction with the Revivent System. Due to rapid developments in cardiac CTA technology, is the image quality and value of CTA almost comparable to the MRI which is the gold standard. The echocardiogram is the most often used method to measure LVEF. This technique has auditory, technical and operator limitations. The LV volume measurement is based on assumption of the LV shape. The measurement of LV volume is not accurate in case of patients with altered LV geometry. Another imaging modality to measure the cardiac function is the radionuclide techniques and invasive contrast ventriculography (CVG). The nuclear imaging has technical limitations and CVG is invasive test with low reliability. New developed and other methods to measure LV volume and LVEF will not be discussed since they lack accuracy . As mentioned earlier, the CTA will be repeated at the end of the study for accurate assessment of the cardiac functional parameters after the operation. We make every effort to avoid unnecessary repeating the CTA. At the moment the radiation dose for cardiac CTA is about 10 millisieverts (mSv). From July 2015, low dose cardiac CTA*s will be possible due the availability of the new scans at AMC . Postoperative will all the patients receive cardiac CT with low dose of radiation.

Risk and Benefit Analysis

Depending on the condition of the patient, the surgeon and the treating cardiologist may recommend that a minimal invasive SVR with the Revivent System be carried out. They believe that it is the most suitable treatment for the patients with benefits which have already been proven. However, all cardiac operations carry certain risks. Some serious complications may even result in death. These complications are typical and anticipated. Although the majority of the following events were not observed in previous studies, the following are considered potential adverse events of the SVR with Revivent System:

* Risks associated with surgery, general anaesthesia, and median sternotomy
* As with any medical device, durability of the implant materials
* Device(s) implanted into the heart that may require removal
* Unintended perforation of the heart wall

* Damage to another structure, such as a valve or the conduction system
* Erosion of the device through adjacent tissue
* Infection due to the presence of a foreign body in the heart tissue
* Patient re-operation that is device-related
* Bleeding
* Embolism
* Mortality
*Radiation induced skin reaction

The risk of this technique is comparable with less-invasive cardiac surgery. Patients who consent to participate will undergo operation and will be required to attend hospital appointments and follow-up exams. MRI has no associated health risks. MRI does not require ionizing radiation, and gadolinium contrast is well tolerated with only very rare cases of gadolinium allergy reported in the literature. For each individual study participant, the MRIs will yield useful information that can be used for the patient*s clinical follow-up. Further, the follow-up will include some routine exams and will be performed in order to evaluate the clinical condition and cardiac function before, during and after the operation. The follow-up period will be 1 year. Clinical evaluation and tests performed during the follow-up period are non-invasive and generally considered standard care for severe heart failure patients. Therefore, there is no specific risk associated with these.

Prior to enrolment, the surgical team will clearly define the indications and contraindications criteria to ensure that only appropriate patients enter the study. The procedure will be performed by one experienced cardiac surgeon. He will ensure that treatment and follow-up are consistent with current medical practice. It is evident that every effort will be made by surgeon to minimize the risks for the patient receiving the Revivent device. The follow-up will allow careful monitoring of each patient, which may lead to prompt treatment adjustments where necessary.
This study will introduce off-pump left ventricular reconstruction using the Revivent System as a potential new treatment option for patients with ischaemic HF. It is expected to reduce the need for implantable cardiac devices, LVADs and heart transplantation, which will lead to decrease in healthcare costs in this group of patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

The following criteria will be applied for inclusion:;- > 18 years of age
- Able to provide written informed consent
- Medical history of antero-septal myocardial infarction with a discreet akinetic/dyskinetic scar located in the antero-septal or apical (may extend laterally) regions of the LV
- Dilated left ventricle with or without aneurysm
- Left ventricular end-systolic volume index (LVESVI) * 60ml/m2
- Left ventricular ejection fraction (LVEF) * 40%
- Symptomatic cardiac dysfunction causing heart failure: NYHA class * II
- Maintenance on stable medical therapy in accordance with prevailing heart failureguidelines
- Mitral valve regurgitation * 1
- With or without cardiac device (ICD/CRT)

Exclusion criteria

Patients are not eligible for the study if they meet the following criteria: ;- Unable or unwilling to provide written informed consent
- * 18 years of age

- Pregnancy or claustrophobia
- Known concomitant disease with a life expectancy of <1 year
- Calcified ventricular wall in the area of intended scar exclusion
- Thrombus or mass in the left atrium or ventricle
- CRT device placement * 60 days prior to surgery
- Thin walled, paradoxically moving septal scar that would preclude successful support of the anchor pairs
- Significant diastolic dysfunction, defined as a pseudo-normal Doppler filling pattern with E/A ratio>2
- Intolerance or unwillingness to take Acenocoumarol
- Functioning pacemaker leads in antero-apical RV, which would interfere with anchor placement
- Pulmonary arterial pressure > 60 mm Hg
- Myocardial infarction within 90 days prior to surgery
- Chronic renal failure with a serum creatinine > 250 µmol/l.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-09-2016
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Revivent Myocardial Anchoring System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL49833.018.14